

SEQUENCE LISTING

<110> ROZEN, Rima

<120> cDNA FOR HUMAN METHYLENETETRAHYDROFOLATE  
REDUCTASE AND USES THEREOF

<130> 04844/005005

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<151> 2000-06-12

<150> US 09/258,928  
<151> 1999-03-01

<150> US 08/738,000  
<151> 1997-02-12

<150> PCT/CA95/00314  
<151> 1995-05-25

<150> GB 9410620.0  
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agt tcg aga tgt tcc acc ccg ggc ctg gac cct gag cgg cat gag aga Ser Ser Arg Cys Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg 35 40 45	144
ctc cgg gag aag atg agg cgg cga ttg gaa tct ggt gac aag tgg ttc Leu Arg Glu Lys Met Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe 50 55 60	192
tcc ctg gaa ttc ttc cct cct cga act gct gag gga gct gtc aat ctc Ser Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu	240

65	70	75	80	
atc tca agg ttt gac	cgg atg gca gca	ggt ggc ccc ctc	tac ata gac	288
Ile Ser Arg Phe Asp	Arg Met Ala Ala	Gly Gly Pro Leu	Tyr Ile Asp	
85	90	95		
gtg acc tgg cac cca	gca ggt gac cct	ggc tca gac aag	gag acc tcc	336
Val Thr Trp His Pro	Ala Gly Asp Pro	Gly Ser Asp Lys	Glu Thr Ser	
100	105	110		
tcc atg atg atc gcc	agc acc gcc gtg aac	tac tgt ggc ctg	gag acc	384
Ser Met Met Ile Ala	Ser Thr Ala Val	Asn Tyr Cys Gly	Leu Glu Thr	
115	120	125		
atc ctg cac atg acc	tgc cgt cag cgc	ctg gag gag	atc acg ggc	432
Ile Leu His Met Thr	Cys Cys Arg Gln	Arg Leu Glu Glu	Ile Thr Gly	
130	135	140		
cat ctg cac aaa gct	aag cag ctg ggc	ctg aag aac atc	atg gcg ctg	480
His Leu His Lys Ala	Lys Gln Leu Gly	Leu Lys Asn Ile	Met Ala Leu	
145	150	155	160	
cg gga gac cca ata	ggt gac cag tgg	gaa gag gag gag	gga ggc ttc	528
Arg Gly Asp Pro Ile	Gly Asp Gln Trp	Glu Glu Glu Gly	Gly Phe	
165	170	175		
aac tac gca gtg gac	ctg gtg aag cac	atc cga agt gag	ttt ggt gac	576
Asn Tyr Ala Val Asp	Leu Val Lys His	Ile Arg Ser Glu	Phe Gly Asp	
180	185	190		
tac ttt gac atc tgt	gtg gca ggt tac	ccc aaa ggc cac	ccc gaa gca	624
Tyr Phe Asp Ile Cys	Val Ala Gly Tyr	Pro Lys Gly His	Pro Glu Ala	
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ggg agc ttt gag gct	gac ctg aag cac	ttg aag gag aag	gtg tct gcg	672
Gly Ser Phe Glu Ala	Asp Leu Lys His	Leu Lys Glu Lys	Val Ser Ala	
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gga gcc gat ttc atc	atc acg cag ctt	ttc ttt gag gct	gac aca ttc	720
Gly Ala Asp Phe Ile	Ile Thr Gln Leu	Phe Glu Ala Asp	Thr Phe	
225	230	235	240	
ttc cgc ttt gtg aag	gca tgc acc gac	atg ggc atc act	tgc ccc atc	768
Phe Arg Phe Val Lys	Ala Cys Thr Asp	Met Gly Ile Thr	Cys Pro Ile	
245	250	255		
gtc ccc ggg atc ttt	ccc atc cag ggc	tac cac tcc ctt	cg gct ctt	816
Val Pro Gly Ile Phe	Pro Ile Gln Gly	Tyr His Ser Leu	Arg Gln Leu	
260	265	270		
gtg aag ctg tcc aag	ctg gag gtg cca	cag gag atc aag	gac gtg att	864
Val Lys Leu Ser Lys	Leu Glu Val Pro	Gln Glu Ile Lys	Asp Val Ile	
275	280	285		
gag cca atc aaa gac	aac gat gct gcc	atc cgc aac tat	ggc atc gag	912
Glu Pro Ile Lys Asp	Asn Asp Ala Ala	Ile Arg Asn Tyr	Gly Ile Glu	
290	295	300		
ctg gcc gtg agc ctg	tgc cag gag ctt	ctg gcc agt ggc	ttg gtg cca	960

Leu Ala Val Ser Leu Cys Gln Glu Leu Leu Ala Ser Gly Leu Val Pro			
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ggc ctc cac ttc tac acc ctc aac cgc gag atg gct acc aca gag gtg			1008
Gly Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val			
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ctg aag cgc ctg ggg atg tgg act gag gac ccc agg cgt ccc cta ccc			1056
Leu Lys Arg Leu Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro			
340	345	350	
tgg gct ctc agt gcc cac ccc aag cgc cga gag gaa gat gta cgt ccc			1104
Trp Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro			
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Ile Phe Trp Ala Ser Arg Pro Lys Ser Tyr Ile Tyr Arg Thr Gln Glu			
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tgg gac gag ttc cct aac ggc cgc tgg ggc aat tcc tct tcc cct gcc			1200
Trp Asp Glu Phe Pro Asn Gly Arg Trp Gly Asn Ser Ser Pro Ala			
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ttt ggg gag ctg aag gac tac tac ctc ttc tac ctg aag agc aag tcc			1248
Phe Gly Glu Leu Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser			
405	410	415	
ccc aag gag gag ctg ctg aag atg tgg ggg gag gag ctg acc agt gaa			1296
Pro Lys Glu Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu			
420	425	430	
gca agt gtc ttt gaa gtc ttt gtt ctt tac ctc tcg gga gaa cca aac			1344
Ala Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn			
435	440	445	
cgg aat ggt cac aaa gtg act tgc ctg ccc tgg aac gat gag ccc ctg			1392
Arg Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu			
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gcg gct gag acc agc ctg ctg aag gag gag ctg ctg cgg gtg aac cgc			1440
Ala Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg			
465	470	475	480
cag ggc atc ctc acc atc aac tca cag ccc aac atc aac ggg aag ccg			1488
Gln Gly Ile Leu Thr Ile Asn Ser Gln Pro Asn Ile Asn Gly Lys Pro			
485	490	495	
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Ser Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe			
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cag aag gcc tac tta gag ttt ttc act tcc cgc gag aca gcg gaa gca			1584
Gln Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala			
515	520	525	
ctt ctg caa gtg ctg aag aag tac gag ctc cgg gtt aat tac cac ctt			1632
Leu Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu			
530	535	540	

gtc aat gtg aag ggt gaa aac atc acc aat gcc cct gaa ctg cag ccg Val Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro 545 550 555 560	1680
aat gct gtc act tgg ggc atc ttc cct ggg cga gag atc atc cag ccc Asn Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro 565 570 575	1728
acc gta gtg gat ccc gtc agc ttc atg ttc tgg aag gac gag gcc ttt Thr Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe 580 585 590	1776
gcc ctg tgg att gag cgg tgg gga aag ctg tat gag gag gag tcc ccc Ala Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Ser Pro 595 600 605	1824
tcc cgc acc atc atc cag tac atc cac gac aac tac ttc ctg gtc aac Ser Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn 610 615 620	1872
ctg gtg gac aat gac ttc cca ctg gac aac tgc ctc tgg cag gtg gtg Leu Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val 625 630 635 640	1920
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acg gag gct cca tgaccctgcg tcctgacgcc ctgcgttga gccactcctg Thr Glu Ala Pro 660	2020
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Leu Arg Glu Lys Met Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe 50 55 60	
Ser Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu 65 70 75 80	
Ile Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp 85 90 95	
Val Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser 100 105 110	
Ser Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr 115 120 125	

Ile Leu His Met Thr Cys Cys Arg Gln Arg Leu Glu Glu Ile Thr Gly  
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 His Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu  
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 Tyr Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala  
 195 200 205  
 Gly Ser Phe Glu Ala Asp Leu Lys His Leu Lys Glu Lys Val Ser Ala  
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 Val Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu  
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 275 280 285  
 Glu Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu  
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 Gly Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val  
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 Leu Lys Arg Leu Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro  
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 Trp Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro  
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 Ile Phe Trp Ala Ser Arg Pro Lys Ser Tyr Ile Tyr Arg Thr Gln Glu  
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 385 390 395 400  
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 Pro Lys Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu  
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 Ala Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn  
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 Arg Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu  
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 515 520 525  
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 Val Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro  
 545 550 555 560  
 Asn Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro  
 565 570 575  
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 580 585 590  
 Ala Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Ser Pro

595	600	605	
Ser Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn			
610	615	620	
Leu Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val			
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Glu Asp Thr Leu Glu Leu Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu			
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Cys Leu Glu Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser
      15          20          25

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cgg gag aag atg agg cg<sup>g</sup> cga ttg gaa tct ggt gac aag tgg ttc tcc 195  
 Arg Glu Lys Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser  
 50 55 60

ctg gaa ttc ttc cct cct cga act gct gag gga gct gtc aat ctc atc 243  
 Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu Ile  
 65 70 75

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tca agg ttt gac cgg atg gca gca ggt ggc ccc ctc tac ata gac gtg 291
Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val
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acc tgg cac cca gca ggt gac cct ggc tca gac aag gag acc tcc tcc 339  
 Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser  
 95 100 105

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atg atg atc gcc agc acc gcc gtg aac tac tgt ggc ctg gag acc atc      387
Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr Ile
110          115          120          125

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ctg cac atg acc tgc tgc cgt cag cgc ctg gag gag atc acg ggc cat 435  
 Leu His Met Thr Cys Cys Arg Gln Arg Leu Glu Glu Ile Thr Gly His  
 130 135 140

ctg cac aaa gct aag cag ctg ggc ctg aag aac atc atg gcg ctg cgg 483  
 Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu Arg

145	150	155	
gga gac cca ata ggt gac cag tgg gaa gag gag gga ggc ttc aac Gly Asp Pro Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe Asn	160	165	531
	170		
tac gca gtg gac ctg gtg aag cac atc cga agt gag ttt ggt gac tac Tyr Ala Val Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr	175	180	579
	185		
ttt gac atc tgt gtg gca ggt tac ccc aaa ggc cac ccc gaa gca ggg Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly	190	195	627
	200	205	
agc ttt gag gct gac ctg aag cac ttg aag gag aag gtg tct gcg gga Ser Phe Glu Ala Asp Leu Lys His Leu Lys Glu Lys Val Ser Ala Gly	210	215	675
	220		
gcc gat ttc atc atc acg cag ctt ttc ttt gag gct gac aca ttc ttc Ala Asp Phe Ile Ile Thr Gln Leu Phe Phe Glu Ala Asp Thr Phe Phe	225	230	723
	235		
cgc ttt gtg aag gca tgc acc gac atg ggc atc act tgc ccc atc gtc Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile Val	240	245	771
	250		
ccc ggg atc ttt ccc atc cag ggc tac cac tcc ctt cgg cag ctt gtg Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu Val	255	260	819
	265		
aag ctg tcc aag ctg gag gtg cca cag gag atc aag gac gtg att gag Lys Leu Ser Lys Leu Glu Val Pro Gln Glu Ile Lys Asp Val Ile Glu	270	275	867
	280	285	
cca atc aaa gac aac gat gct gcc atc cgc aac tat ggc atc gag ctg Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu Leu	290	295	915
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gcc gtg agc ctg tgc cag gag ctt ctg gcc agt ggc ttg gtg cca ggc Ala Val Ser Leu Cys Gln Glu Leu Leu Ala Ser Gly Leu Val Pro Gly	305	310	963
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ctc cac ttc tac acc ctc aac cgc gag atg gct acc aca gag gtg ctg Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val Leu	320	325	1011
	330		
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gct ctc agt gcc cac ccc aag cgc cga gag gaa gat gta cgt ccc atc Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro Ile	350	355	1107
	360	365	
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	380		
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Asp Glu Phe Pro Asn Gly Arg Trp Gly Asn Ser Ser Ser Pro Ala Phe			
385	390	395	
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Gly Glu Leu Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser Pro			
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Lys Glu Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu Ala			
415	420	425	
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Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn Arg			
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aat ggt cac aaa gtg act tgc ctg ccc tgg aac gat gag ccc ctg gcg			1395
Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu Ala			
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Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg Gln			
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Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe Gln			
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Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala Leu			
510	515	520	525
ctg caa gtg ctg aag aag tac gag ctc cgg gtt aat tac cac ctt gtc			1635
Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu Val			
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Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro Asn			
545	550	555	
gct gtc act tgg ggc atc ttc cct ggg cga gag atc atc cag ccc acc			1731
Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro Thr			
560	565	570	
gta gtg gat ccc gtc agc ttc atg ttc tgg aag gac gag gcc ttt gcc			1779
Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe Ala			
575	580	585	
ctg tgg att gag cgg tgg gga aag ctg tat gag gag gag tcc ccg tcc			1827
Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Glu Ser Pro Ser			
590	595	600	605
cgc acc atc atc cag tac atc cac gac aac tac ttc ctg gtc aac ctg			1875
Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn Leu			
610	615	620	

gtg gac aat gac ttc cca ctg gac aac tgc ctc tgg cag gtg gtg gaa	1923
Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val Glu	
625	630
635	
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Asp Thr Leu Glu Leu Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu Thr	
640	645
650	
gag gct cca tga ccctgcgtcc tgacgccctg cgttggagcc actcctgtcc	2023
Glu Ala Pro *	
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Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser Met Met Ile	
100 105 110	
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115 120 125	
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180 185 190	
Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly Ser Phe Glu	
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 Pro Asn Gly Arg Trp Gly Asn Ser Ser Pro Ala Phe Gly Glu Leu  
 385 390 395 400  
 Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser Pro Lys Glu Glu  
 405 410 415  
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 420 425 430  
 Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn Arg Asn Gly His  
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